Non Cirrhotic Portal Fibrosis

*Ralph Girson *, Andri Sanityoso **, Rino A Gani ***
*Wirasmi Marwoto ***, Murdani Abdullah****, Ari F Syam *****

*Department of Internal medicine, Faculty of medicine University of Indonesia/
Dr. Cipto Mangunkusumo General National Hospital
** Division of Hepatology, Department of Internal Medicine, Faculty of Medicine,
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
***Department of Pathology Anatomy, Faculty of Medicine,
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
**** Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital

ABSTRACT

Diagnosis of non cirrhotic portal fibrosis was considered when the following criteria were fulfilled evidence of portal hypertension (oesophageal varices, hypersplenism, ascites, or increased hepatic venous pressure gradient), Doppler ultrasound showing patent portal and hepatic veins, and liver biopsy showing sign of cirrhosis. Non cirrhotic portal fibrosis clinically characterized by splenomegaly, anemia, portal hypertension, and histopathological examination portal tract showing fibrosis and sclerosis. Portal hypertension are most caused by a cirrhotic liver (85%), there are only a few reports on non cirrhotic portal hypertension, mostly in Japan and India. We reported a case of non cirrhotic portal fibrosis in young male. The clinical complications of portal hypertension are variceal bleeding and pancytopenia due to hypersplenism. Variceal band ligation and splenectomy were performed. The patient showed good clinical response.

Keywords: *portal hypertension, non cirrhotic portal fibrosis, young male*

INTRODUCTION

The standard of normal portal venous pressure is 5 - 10 mmHg. Portal hypertension is defined as pressure that exceeds 10 mmHg.[1-4] Cirrhosis is the most common cause of portal hypertension in the United States (85%). Other causes of portal hypertension are portal vein obstruction, infection, pancreatitis, abdominal trauma, portal vein thrombosis or idiopathic. Idiopathic portal vein thrombosis may develop in a variety of hypercoagulable states, including polycthemia vera, essential trombocythemia, deficiency of protein C, protein S or antithrombin III.[3] Hepatic vein thrombosis and hepatic venoocclusive disease are relatively infrequent cause of portal hypertension. Non cirrhotic portal fibrosis accounts for only a few cases of portal hypertension. There are reports on non-cirrhotic portal hypertension in India and Japan, and in Indonesia it is presumed to be less than 5%.[2, 3]

Causes of portal hypertension can be classified as increased resistance to flow and increase portal blood flow. Increasing resistance can cause by at pre-hepatic obstruction (portal vein obstruction), intrahepatic obstruction, and posthepatic obstruction.

Non cirrhotic fibrosis of the liver can be distinguished from cirrhosis by the absence of hepatocellular damage and lack of nodular regenerative activity, but there are still manifestations of portal hypertension. There are three variants of Idiopathic Portal Hypertension or Non Cirrhotic Portal Fibrosis (NCPF) as follows:

Diagnosis of NCPF was considered when the following criteria were fulfilled: evidence of portal hypertension (oesophageal varices, hypersplenism, ascites, or increased hepatic venous pressure gradient). Doppler ultrasound showing patent portal and hepatic veins, liver biopsy showing no cirrhosis.[6] Non cirrhotic portal fibrosis (NCPF) clinically characterized by

Table1. Causes of Portal Hypertension[5]

Increased Resistance Below		
Prehepatic (portal vein obstruction) • Congenital atresia or stenosis • Thrombosis of portal vein • Thrombosis of splenic vein • Extrinsic compression (for example tumours)	*Hepatic* • Cirrhosis • Acute alcoholic liver disease • Congenital hepatic fibrosis • Idiopathic portal hypertension (hepatoportal sclerosis) • Idiopathic portal hypertension (hepatoportal sclerosis) • Schitosomiasis	*Posthepatic* • Budd-Chiari syndrome • Constrictive pericarditis
Increased Portal Blood Flow • Arterial-portal venous fistula Increased splenic flow		

Table 2. Some Causes of Non cirrhotic Hepatic Fibrosis[3]

Idiopathic portal hypertension (non cirrhotic portal fibrosis, Banti's syndrome); three variants:
Intrahepatic phlebosclerosis and fibrosis
Portal and splenic vein sclerosis
Portal and splenic vein thrombosis
Schistosomiasis ("pipe-stem" fibrosis with presinusoidal portal hypertension)
Congenital hepatic fibrosis (may be associated with polycystic disease of liver and kidneys)

splenomegaly, anemia, portal hypertension and histologically by portal tract fibrosis and sclerosis. NCPF is a common cause of portal hypertension in India.[6]

The major clinical manifestations of portal hypertension include haemorrhage from gastro-esophageal varices, splenomegaly with hypersplenism, ascites, and acute and chronic hepatic encephalopathy.[3] Treatments are directed to specific manifestations of portal hypertension, and sometimes to reduce the pressure in the portal venous system. Both surgery and β-adrenergic blockade can reduce the portal hypertension. The focus on treatments are lowering the portal pressure which can be measured in wedge hepatic vein pressure < 12 mmHg, or by 20% from baseline. If wedged hepatic pressure is not feasible, reduction of 25% heart rate is reasonable.[3]

This case report of a young male 17 years old with a blood vomiting, caused by oesophageal varices, and hypersplenism caused by massive splenomegaly. Both were complications of NCPF. Ligation and splenectomy were performed and the results were good condition after these procedure.

CASE ILLUSTRATION

Male, 17 years old was admitted to our hospital on 12th of December 2004 with chief complaint of hematemesis 3 months prior to admission. Patient had no fever. He also complained of general weakness. There was no complaint of cough or night sweat.

He had history of hematemesis and melena since 4 months and 3 months before admission. He was first hospitalized at other hospital. In this hospital ultra sound examination and endoscopy were done. The ultra sound's result was chronic liver disease and splenomegaly. Endoscopy revealed oesophageal varices grade III-IV. He was then referred to our hospital for variceal ligation.

Four years before, patient felt swelling on his left upper abdomen. He did not feel any pain, although the size of the swelling was getting bigger. Since the patient did not consider his ill seriously, he did not see the doctor.

He and his family have no history of liver disease, and or icteric, no history of malaria, or travelling to endemic area. He is experiencing his social life as a high school student. His father has died several years ago. Never use any drugs, alcohol, traditional medicine, nor herbal medicine.

On physical examination we found good general condition, under nutrition with BMI 16.7 kg/m^2. Pressure was 120/80 mmHg, pulse rate 90 x/m, respiratory rate 20 x/m, temperature 36°C. His conjunctiva did not look pale, and not icteric, there is no abnormality found in heart and lungs examination. From abdominal examination we found no abnormality except the spleen was enlarged (Schufner V) and there was no abdominal tenderness.

Laboratory results revealed hemoglobin 9.2 g/dL (13-16), hematocryte 29.6% (40-48), leukocyte 3,000/μL (5,000-10,000), trombocyte 57,000/μL (150,000-400,000 μL), MCV 76.7 fL MCH 23.8 pg MCHC 31.1 g/dL, ALT 12 U/L (0-35), AST 24 U/L (0-36), normal urine analysis, albumin level of 4.2 g/dL (3,4-4,8), globulin level of 3 g/dL (1.8-3.9), total bilirubin level of 1.0 mg/dL (0.0-1.0), direct bilirubin level of 0.3 mg/dL (0.0-0.3), indirect bilirubin level of 0.7 mg/dL (0.0-0.7), sodium concentration of 141 mEq/L (135-147), potassium concentration of 3.92 mEq/L (3.5-5.5), chloride 106 mEq/L (100-106), BUN 17 mg/dL (10-50), creatinin 0.5 mg/dL (0.5-1.5), random blood glucose 105 mg/dL. Chest X-ray examination was normal.

There were several problems in this patient, first oesophageal varices with history of variceal bleeding. The second problem was splenomegaly with pancytopenia, which considered as hypersplenism. These problems were considered as one entity of portal hypertension. Portal hypertension in this patient was considered as non cirrhotic portal hypertension. We have further using diagnostic procedure to determine the etiology of portal hypertension. We plan to use ultrasound with doppler, liver biopsy examination of hepatitis B marker, hepatitis C marker. We plan to use bone marrow puncture to confirm hypersplenism as an etiology of pancytopenia

Bone marrow puncture and biopsy were done, and the result has shown no abnormality in his bone marrow, and it was considered as hypersplenism. Ultrasound and Doppler were used and the results were splenomegaly, normal liver's size, and thrombus in splenic vein and portal vein. Hepatitis C marker (anti HCV) was negative and hepatitis B (HBsAg, anti HBc IgM, HBV DNA) were also negative. Liver biopsy revealed portal fibrosis, liver fibrosis stadium 2, and weak positive on immunoperoxyde staining.

Due to portal vein thrombus and splenic vein thrombus we did measure of protein C, protein S, coagulation study and the result were protein C 158.6% (70 - 140) and protein S 120% (70 - 123), dimer 1,500 ng/mL (0 - 300), fibrinogen 176 mg/dL, (200 - 400), prothrombin time (PT) 17.3 second (11 - 14) activated partial thrombin time (aPTT) 40.6 second (25.6 - 35.2).

Portal hypertension in this patient were treated with pharmacological propanolol 2 x 10 mg and isosorbide mononitrate 2 x 10 mg. Blood pressure 110/70 mmHg and heart rate was 70 x/m after propanolol and isosorbide mononotrate. We plan band ligation due to oesophageal varices. We plan to apply splenectomy procedure due to hypersplenism.

During splenectomy operation, liver biopsy, and lien biopsy were taken during the operation, and histopathological examination was done. The histopathological result was fibrosis liver grade 3, no sign of metastases and positive for viral hepatitis B. Histopathological of spleen was considered as fibrocongestive spleen.

There is no complication during and after the operation. After operation patient's condition was stable. His final blood test after operation was haemoglobin 11 g/dL (13-16), hematocryt 35.2% (40-48), leukocyte 9,500 u/L, thrombocyte 710,000/uL (150,000 - 400,000). The patient was discharged from hospital in stable condition and had regular visit at hepatology and gastroenterology outpatient clinic.

DISCUSSION

Male patient, 17 years old, with history of hematemesis and caused by oesophageal varices bleeding. His problem was portal hypertension and the manifestations are oesophageal varices and splenomegaly. Complications were variceal bleeding and hypersplenism. He was admitted due to these complications.

Diagnosis of portal hypertension is portal pressure that exceeds 10 mmHg. Measuring the portal vein pressure can be done directly or indirectly.[1] Direct measurement is performed by inserting a catheter into the portal vein or one of it branches. Indirect measurement is performed by inserting a catheter into antecubital or femoral vein, and then advance to the small hepatic vein, the pressure is subtracted from free hepatic venous pressure to intra abdominal pressure. Indirect method is safe and simple than direct procedure but it may not accurate if portal flow block before it enter the sinusoids.[7] Portal hypertension clinically can be revealed by the appearance of splenomegaly, ascites, encephalopathy, and or oesophageal varices.[1,3,7] CO_2 weged hepatic venography can make distinction to presinusoidal portal hypertension and sinusoidal portal hypertension.[8]

Portal hypertension in this patient was based on clinical features. The clinical manifestations were oesophageal varices, splenomegaly, and thrombosis portal vein, thrombosis splenic vein. We did not measure portal vein pressure because we think it would not change treatment in this patient.

Most portal hypertension conditions have underlying cirrhosis liver. However, we were doubtful this patient had cirrhotic portal hypertension because his general condition was good except slightly undernourished. There were no signs of cirrhosis found such as erythema palmaris, spider nevi, ascites, or collateral vein. His albumin serum and also other liver function test were normal. Histopathological on his liver showed that portal

fibrosis and fibrosis liver grade 3. Cirrhosis as a cause of portal hypertension can be excluded in this condition.

Non cirrhotic portal fibrosis are clinically characterized by splenomegaly, anemia and portal hypertension, and histologically by portal tract fibrosis and sclerosis.[9-10] Diagnosis of non cirrhotic portal hypertension was considered when following criteria fulfilled evidence of portal hypertension, Doppler ultrasound showing patent portal and hepatic veins, no cirrhosis from liver biopsy, and exclusion of conditions causing cirrhosis such as chronic viral hepatitis, alcoholic liver disease, non alcoholic steatohepatitis, obesity.[11] Therefore this patient was diagnosed non cirrhotic portal fibrosis.

The Doppler ultrasonography had shown that this patient had thrombosis at the portal vein and splenic vein. Thrombosis at the portal vein and or splenic vein as a causative in portal hypertension is still controversial.[9,12] Portal vein thrombosis are associated with systemic or local infections (e.g. cholangitis, phlebitis), cirrhotic, hepatocarcinoma, hypercoagulable (protein C, protein S, antithrombin III deficiency). Portal vein thrombosis reported in India was idiopathic, regarding to normal anticoagulant natural level.[13] Protein C and protein S level this patient is normal, prothrombin time is normal, therefore we concluded that portal vein thrombosis was secondary to portal hypertension or portal fibrosis.

We found this patient had non cirrhotic portal fibrosis based on evidence of portal hypertension, oesophageal varices, and splenomegaly, no sign of eritema palmaris-spider naevi, normal liver function on blood test (transaminases, albumin), and portal fibrosis on histopathological. There are number of hypotheses have been proposed for the ethiopathogenesis; infection, exposure of chemicals or trace metals, immunologic or immunogenetic. Umbilical sepsis bacterial infections and diarrhoeal episodes in infancy and early childhood are likely to lead to portal pyemia, pylephlebitis, resulting in thrombosis, sclerosis and obstruction of small and medium sized portal vein radicals.[14] Hepatitis B marker was negative in this patient, while the histopathological showed hepatitis B. We considered that possible cause of portal fibrosis was non specific bacteria infections.

Clinical complications of portal hypertension are gastrointestinal bleeding, hepatic encephalopathy, ascites, spontaneous bacterial peritonitis, and hepatopulmonary syndrome.[1] Patient's managements depend on complication of portal hypertension. This patient had oesophageal varices bleeding, and hypersplenism. The key management issues in patients with NCPF are gastrointestinal bleeding and hypersplenism.[14] The management of this patient was focused on these complications with band ligation endoscopic, and splenectomy.

Treatment strategies for oesophagastric varices are pharmacologic therapy, endoscopic therapy, tamponade, decompression surgical, devascularization operation and liver transplantation.[7] Propanolol and isosorbide mononitrate as pharmacological treatment were given to lowering the portal pressure. β-blocker (propanolol) as primary prophylaxis had shown a significant reduction in incidence of first variceal haemorrhage. β-blocker are indicated in all patients who are high risk of variceal haemoerhage. The risk are HVPG > 12 mmHg, red sign on varices, child class, continued alcohol abuse, varices size.[1] Combination of propanolol and isosorbide mononitrate is effective in lowering portal pressure.[15]

Patient admitted was not in the variceal bleeding, therefore pharmacologic therapy, and then band ligation was performed. Propanolol 10 mg twice daily, and isosorbide mononitrate 20 mg twice daily, were given and his heart rate was reducing about 20%. Propanolol are safe and effective as the first treatment of choice.[16-18] Combination of propanolol and isosorbide mononitrate needs further evaluation, because this combination have not been confirmed in NCPF patients.[18]

Oesophageal varices in NCPF are rarely requiring surgical intervention. Transjugular intrahepatic porto systemic shunt (TIPS) procedure has been reported to be effective in idiopathic portal hypertension, however TIPS has been done in a small number NCPF patients. Generally the studies have shown lower incidence of recurrent bleeding in TIPS, but higher rates of encephalopathy were reported in TIPS.[7,13,16,17] TIPS currently is not recommended for the routine prevention of rebleeding.[17] TIPS cannot be performed due to portal vein thrombosis.[17]

Surgery is an effective alternative treatment to endoscopic therapy. Surgery is also indicated for patients with symptomatic hypersplenism, spontaneous bleeding or severe anemia requiring transfusion or splenic infarcts.[14] Devascularization procedures have the components of splenectomy, gastric and oesophageal devascularization, with the goal of reduced blood flow to oesophageal varices.[7]

Endoscopic ligation is the first line procedure in the management of variceal bleeding in cirrhotic because it is more effective and safer.[16,17] Ligation was performed, but recurrent bleeding occurred, then another ligation was done. Splenectomy procedure was treatment of choice in this patient because of recurrent pancytopenia due to hypersplenism.

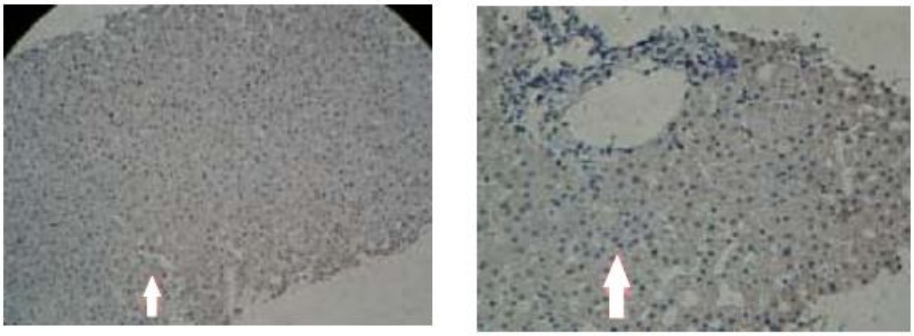

Figure 1. Liver biopsy revealed portal fibrosis, liver fibrosis stadium 2, and weak positive on immunoperoxyde staining

Figure 2. Pictures of his spleen, taken with splenectomy procedure

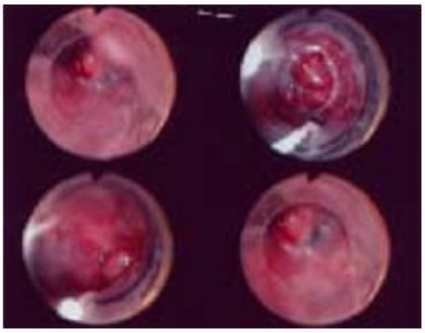

Figure 3. The endoscopy shown esophagus varices during multiband ligation

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